# Refine Search

**Search Results -**

| Term | Documents |
|---|---|
| PEROXIDE | 232389 |
| PEROXIDES | 55334 |
| ARGININE | 56505 |
| ARGININES | 847 |
| (29 AND ARGININE AND PEROXIDE).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD. | 3 |
| (L29 AND "PEROXIDE" AND "ARGININE" ).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD. | 3 |

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**Search:**

Refine Search | Recall Text | Clear | Interrupt

## Search History

**DATE: Thursday, May 13, 2004** Printable Copy Create Case

| Set Name side by side | Query | Hit Count | Set Name result set |
|---|---|---|---|
| *DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR* | | | |
| L30 | L29 and "peroxide" and "arginine" | 3 | L30 |
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| L28 | L27 and "peroxide" and "arginine" | 7 | L28 |
| L27 | "Lactobacillus casei" and "Lactobacillus fermentum" | 133 | L27 |
| L26 | L25 and "hydrogen peroxide" and "arginine" | 6 | L26 |
| L25 | "Lactobacillus casei" and "Lactobacillus gasseri" | 78 | L25 |
| L24 | L21 and "Lactobacillus gasseri" | 8 | L24 |

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| | | | |
|---|---|---|---|
| L23 | l21 and "Lactobacillus fermentum" | 10 | L23 |
| L22 | L21 and "Lactobacillus brevis" | 6 | L22 |
| L21 | L20 and "hydrogen peroxide" | 94 | L21 |
| L20 | L19 and "arginine" | 153 | L20 |
| L19 | "Lactobacillus" and "peroxide" | 637 | L19 |
| L18 | L17 and "arginine" | 5 | L18 |
| L17 | L16 and "Lactobacillus" | 7 | L17 |
| L16 | "DSM 11988" | 7 | L16 |
| *DB=USPT; PLUR=YES; OP=OR* | | | |
| L15 | L8 and "Lactobacillus fermentum" | 4 | L15 |
| L14 | L8 and "Lactobcillus gasseri" | 0 | L14 |
| L13 | L8 and "Lactobacillus brevis" | 0 | L13 |
| L12 | L8 and "arginine" | 0 | L12 |
| L11 | L8 and "arginine" | 0 | L11 |
| L10 | l8 and "Lactobacillus crispatus" | 4 | L10 |
| L9 | L8 and "Lactobacillus salivarius" | 1 | L9 |
| L8 | "Lactobacillus" and "hydrogen peroxide producing" | 15 | L8 |
| L7 | L6 and "lactobacillus" | 19 | L7 |
| L6 | Cavaliere Ved. Vesely.in. | 453 | L6 |
| L5 | 6277340.pn. | 1 | L5 |
| L4 | 62773470.pn. | 0 | L4 |
| L3 | 6273470.pn. | 1 | L3 |
| L2 | 2773470.pn. | 1 | L2 |
| L1 | 6773470.pn. | 0 | L1 |

END OF SEARCH HISTORY

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| L5 | 6277340.pn. | 1 | L5 |
| L4 | 62773470.pn. | 0 | L4 |
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| L2 | 2773470.pn. | 1 | L2 |
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**Search Results** - Record(s) 1 through 10 of 15 returned.

☐ 1. Document ID: US 6479045 B2

L8: Entry 1 of 15 File: USPT Nov 12, 2002

US-PAT-NO: 6479045
DOCUMENT-IDENTIFIER: US 6479045 B2

TITLE: Vaginal pH buffering for preventing miscarriage and premature labor, by treating or preventing bacterial vaginosis

DATE-ISSUED: November 12, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Bologna; William J. | Paris | | | FR |
| Levine; Howard L. | Oceanside | NY | | |

US-CL-CURRENT: 424/78.08; 424/400, 424/422, 424/430, 424/434, 424/436, 424/451, 424/464, 424/78.17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 6468526 B2

L8: Entry 2 of 15 File: USPT Oct 22, 2002

US-PAT-NO: 6468526
DOCUMENT-IDENTIFIER: US 6468526 B2

TITLE: Vaginal lactobacillus medicant

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Chrisope; Gerald L. | Boulder | CO | | |

US-CL-CURRENT: 424/93.45; 435/243, 435/252.1, 435/252.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 3. Document ID: US 6372209 B1

L8: Entry 3 of 15 File: USPT Apr 16, 2002

US-PAT-NO: 6372209
DOCUMENT-IDENTIFIER: US 6372209 B1

TITLE: Vaginal lactobacillus medicant

DATE-ISSUED: April 16, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Chrisope; Gerald L. | Boulder | CO | | |

US-CL-CURRENT: 424/93.45; 435/243, 435/252.1, 435/252.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 4. Document ID: US 6165493 A

L8: Entry 4 of 15 File: USPT Dec 26, 2000

US-PAT-NO: 6165493
DOCUMENT-IDENTIFIER: US 6165493 A

TITLE: "Methods and compositions for decreasing the frequency of HIV, herpesvirus and sexually transmitted bacterial infections"

DATE-ISSUED: December 26, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Neurath; Alexander Robert | New York | NY | | |
| Jiang; Shibo | Jackson Heights | NY | | |
| Debnath; Asim Kumar | New York | NY | | |
| Strick; Nathan | Oceanside | NY | | |
| Dow; Gordon Jay | Santa Rosa | CA | | |

US-CL-CURRENT: 424/434; 424/430, 424/431, 424/432, 424/433, 424/435, 424/436, 424/443, 424/494

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 5. Document ID: US 6093394 A

L8: Entry 5 of 15 File: USPT Jul 25, 2000

US-PAT-NO: 6093394
DOCUMENT-IDENTIFIER: US 6093394 A

h e b b g e e e f e ef b e

TITLE: Vaginal lactobacillus medicant

DATE-ISSUED: July 25, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Chrisope; Gerald L. | Boulder | CO | | |

US-CL-CURRENT: 424/93.45; 435/243, 435/252.1, 435/252.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 6. Document ID: US 6004551 A

L8: Entry 6 of 15 File: USPT Dec 21, 1999

US-PAT-NO: 6004551
DOCUMENT-IDENTIFIER: US 6004551 A

TITLE: Lactobacillus and skim milk pharmaceutical compositions

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Reid; Gregor | London | | | CA |
| Bruce; Andrew W. | Toronto | | | CA |

US-CL-CURRENT: 424/93.45; 424/430, 424/535, 435/244, 435/252.9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 7. Document ID: US 5958461 A

L8: Entry 7 of 15 File: USPT Sep 28, 1999

US-PAT-NO: 5958461
DOCUMENT-IDENTIFIER: US 5958461 A

TITLE: Vaginal pharmaceutical compositions

DATE-ISSUED: September 28, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Larsen; Bryan | Huntington | WV | | |

US-CL-CURRENT: 424/614

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 8. Document ID: US 5876990 A

L8: Entry 8 of 15 File: USPT Mar 2, 1999

US-PAT-NO: 5876990
DOCUMENT-IDENTIFIER: US 5876990 A

TITLE: Biochemical media system for reducing pollution

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Reddy; Malireddy S. | Englewood | CO | 80110 | |
| Reddy; Syama M. | Englewood | CO | 80110 | |

US-CL-CURRENT: 435/177; 210/606, 210/611, 210/632, 252/180, 252/181, 426/53, 435/262

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 9. Document ID: US 5840744 A

L8: Entry 9 of 15 File: USPT Nov 24, 1998

US-PAT-NO: 5840744
DOCUMENT-IDENTIFIER: US 5840744 A
**** See image for Certificate of Correction ****

TITLE: Intravaginal treatment of vaginal infections with buffered metronidazole compositions

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Borgman; Robert J. | Mundelein | IL | | |

US-CL-CURRENT: 514/398; 514/944, 514/967

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 10. Document ID: US 5804179 A

L8: Entry 10 of 15 File: USPT Sep 8, 1998

US-PAT-NO: 5804179
DOCUMENT-IDENTIFIER: US 5804179 A
**** See image for Certificate of Correction ****

h e b b g e e e f e ef b e

TITLE: Lactobacillus compositions and methods for treating urinary tract infections

DATE-ISSUED: September 8, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Bruce; Andrew W. | Toronto | | | CA |
| Reid; Gregor | London | | | CA |

US-CL-CURRENT: 424/93.45; 435/252.9, 435/853, 435/854, 435/855, 435/856, 435/857





| Term | Documents |
|---|---|
| LACTOBACILLUS | 3410 |
| LACTOBACILLU | 5 |
| "HYDROGEN PEROXIDE PRODUCING" | 0 |
| (LACTOBACILLUS AND "HYDROGEN PEROXIDE PRODUCING").USPT. | 15 |
| ("LACTOBACILLUS" AND "HYDROGEN PEROXIDE PRODUCING").USPT. | 15 |



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# Hit List

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**Search Results** - Record(s) 11 through 15 of 15 returned.

☐ 11. Document ID: US 5778886 A

L8: Entry 11 of 15 File: USPT Jul 14, 1998

US-PAT-NO: 5778886
DOCUMENT-IDENTIFIER: US 5778886 A

TITLE: Vaginal compositions combining a spermicidal agent and a peroxygen compound

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Shihata; Alfred | Del Mar | CA | 92014 | |

US-CL-CURRENT: 128/832; 128/830, 424/430

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 12. Document ID: US 5705160 A

L8: Entry 12 of 15 File: USPT Jan 6, 1998

US-PAT-NO: 5705160
DOCUMENT-IDENTIFIER: US 5705160 A

TITLE: Lactobacillus compositions and methods for treating urinary tract infections

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Bruce; Andrew W. | Toronto | | | CA |
| Reid; Gregor | London | | | CA |

US-CL-CURRENT: 424/93.45; 435/252.9, 435/853, 435/857

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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☐ 13. Document ID: US 5645830 A

L8: Entry 13 of 15 File: USPT Jul 8, 1997

US-PAT-NO: 5645830
DOCUMENT-IDENTIFIER: US 5645830 A

TITLE: Lactobacillus and skim milk compositions and methods for preventing microbial urogenital infections

DATE-ISSUED: July 8, 1997

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Reid; Gregor | London | | | CA |
| Bruce; Andrew W. | Toronto | | | CA |

US-CL-CURRENT: 424/93.45; 424/430, 424/535, 435/252.9, 435/853, 435/854, 435/855, 435/856, 435/857, 514/968

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 14. Document ID: US 5536743 A

L8: Entry 14 of 15 File: USPT Jul 16, 1996

US-PAT-NO: 5536743
DOCUMENT-IDENTIFIER: US 5536743 A
**** See image for Certificate of Correction ****

TITLE: Intravaginal treatment of vaginal infections with buffered metronidazole compositions

DATE-ISSUED: July 16, 1996

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Borgman; Robert J. | Mundelein | IL | | |

US-CL-CURRENT: 514/398; 514/944, 514/967

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 15. Document ID: US 4912047 A

L8: Entry 15 of 15 File: USPT Mar 27, 1990

US-PAT-NO: 4912047
DOCUMENT-IDENTIFIER: US 4912047 A
**** See image for Certificate of Correction ****

h e b b cg b cc e

TITLE: Preventing psychrotrophic bacterial spoilage in raw milk

DATE-ISSUED: March 27, 1990

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Matrozza; Mark A. | Sarasota | FL | | |
| Leverone; Marianne F. | Bradenton | FL | | |
| Boudreaux; Donald P. | Sarasota | FL | | |

US-CL-CURRENT: 435/252.9; 426/330.2, 426/61, 435/856





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| LACTOBACILLUS | 3410 |
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| "HYDROGEN PEROXIDE PRODUCING" | 0 |
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L8: Entry 10 of 15 File: USPT Sep 8, 1998

DOCUMENT-IDENTIFIER: US 5804179 A
**** See image for Certificate of Correction ****
TITLE: Lactobacillus compositions and methods for treating urinary tract infections

Abstract Text (1):
This invention relates to lactobacillus compositions and methods of employing said compositions for treating or preventing urinary tract infections. More particularly, this invention relates to the ability of certain strains of lactobacilli to adhere to uroepithelial or vaginal epithelial cells and to exhibit inhibitory activity against the growth of pathogenic bacteria.

Brief Summary Text (9):
The present invention provides a method for the treatment or prevention of urinary tract infections of mammals including humans which comprises administering a safe and effective amount of one or more lactobacillus viable whole cells, non-viable whole cells, cell wall fragments or inhibitory substances. The lactobacillus is of one or more species of lactobacillus which adheres to uroepithelial or vaginal epithelial cells.

Brief Summary Text (14):
Also defined within the present invention are compositions suitable for treating or preventing urinary tract infections of mammals including humans which comprise one or more lactobacillus viable whole cells, non-viable whole cells, cell wall fragments or inhibitory substances and a pharmaceutically acceptable carrier, wherein the lactobacillus is of one or more species of lactobacillus which adheres to uroepithelial or vaginal epithelial cells.

Brief Summary Text (16):
In a preferred aspect, the lactobacillus is aerobically or microaerophilically grown and may be selected from the group consisting of Lactobacillus casei, L. acidophilus, L. plantarum, L. fermentum, L. brevis, L. jensenii and L. crispatus.

Brief Summary Text (17):
More specifically, the lactobacillus may be aerobically grown and is selected from the group consisting of Lactobacillus casei var rhamnosus GR-1 (ATCC 55826), L. casei var rhamnosus GR-2 (ATCC 55915), L. casei var rhamnosus GR-3 (ATCC 55917), L. casei var rhamnosus GR-4 (ATCC 55916), L. casei var rhamnosus RC-9, L. casei var rhamnosus RC-17 (ATCC 55825), L. casei var alactosus RC-21, L. casei NRC 430 and L. casei ATCC 7469.

Brief Summary Text (18):
Alternatively, the lactobacillus may be microaerophilically grown and selected from the group consisting of L. plantarum RC-12 (ATCC 55895), L. acidophilus RC-25, L. plantarum RC-19, L. jensenii RC-11 (ATCC 55901), L. acidophilus ATCC 4357 L. plantarum ATCC 8014, L. fermentum A-60, and L. fermentum B-54 (AICC 55920).

Brief Summary Text (19):
In a preferred form of the present invention, the lactobacillus is selected to be substantially resistant to spermicide. Details are provided hereinbelow.

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Brief Summary Text (21):
Although this invention is not intended to be limited to any particular mode of application, intravaginal, intraurethral or periurethral installation of the compositions are preferred. The compositions may be installed in the form of a cream, liquid, paste, gel or suppository as desired. One preferred form is a cream formulation comprising one or more lactobacillus viable whole cells, non-viable whole cells, cell wall fragments or inhibitory substances in a jelly base, preferably a K-jelly base. Another preferred form of application involves the preparation of a freeze-dried capsule comprising the composition of the present invention. It has been found that a capsule comprising /10.sup.9 organisms is suitable.

Brief Summary Text (22):
By "safe and effective amount" as used herein is meant an amount of lactobacillus high enough to significantly positively modify the condition to be treated but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. A safe and effective amount of lactobacillus will vary with the particular condition being treated, the age and physical condition of the patient being treated, the severity of the condition, the duration of treatment, the nature of concurrent therapy, and the specific lactobacillus employed. We have found that at least 10 lactobacilli, and preferably 20 to 30, and more preferably more than 40 said bacteria adhered to epithelial cells are desired. The effective amount of lactobacillus will thus be the minimum amount which will provide the desired attachment to epithelial cells. The presence of 5.times.10.sup.9 bacteria, as viable or non-viable whole cells, in 0.05 ml. solution of phosphate buffered saline solution, or in 0.05 ml. of suspension of agar, or the dry weight equivalent of cell wall fragments, has been found effective when administered in quantities of from about 0.05 ml. to about 20 ml.

Brief Summary Text (27):
Accordingly, in a further aspect of this invention, a novel method of treating or preventing urinary tract infections is provided which involves coating a biologically compatible prosthetic device with a safe and effective amount of one or more of lactobacillus viable whole cells, non-viable whole cells, cell wall fragments or inhibitory substances and inserting the device into the urogenital tract.

Brief Summary Text (29):
Very successful coverage of such devices with the lactobacillus of the present invention has been achieved.

Brief Summary Text (30):
Accordingly, in a preferred form of treatment of urinary tract infections or the prevention of urinary tract infections, the patient is administered a safe and effective amount of a lactobacillus composition in accordance with the present invention, for example, periurethrally, and is then installed with a prosthetic device pre-coated with the lactobacillus viable whole cells, non-viable whole cells, cell wall fragments or inhibitory substances of the present invention. Alternatively, the prosthetic device may not be pre-coated but may be inserted into a patient having been administered a, for example, periurethral pre-coat of the lactobacillus composition described above. With the administration of the composition prior to prosthetic device insertion, an indigenous protective flora is formed which may effectively compete with uropathogens emerging as a result of antibiotic selection or other natural events.

Brief Summary Text (31):
Although the normal microbial flora of the vagina in the maintenance of a healthy state is not completely understood, it is believed that Lactobacillus species play a part in the protection against colonization by pathogenic microorganisms. It has been found that women with a history of urinary tract infections have a urogenital

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flora dominated by pathogens whereas lactobacilli predominate in healthy women. The ecological balance of the vagina can be upset in a number of ways, including the prolonged use of antibiotics and pregnancy. In addition, researchers have implicated the diaphragm as a predisposing factor in recurrent urinary tract infections (Fihn S. D., Latham R. H., Roberts P., Running K., Stamm W. E. 1985 Association between diaphragm use and urinary tract infection J. Am. Med. Assoc. 254: 240-245). A number of studies have found that women using this form of contraception are between 1.5 and 4.1 times more likely to develop urinary tract infection. It has been suggested that increased pressure of the diaphragm on the female urethra may be in part responsible for this. However, the diaphragm is usually used in conjunction with a spermicidal cream or foam and these preparations have been found to have a bactericidal effect on some protective bacteria such as lactobacillus. In addition, it has been found that some uropathogens, such as Candida sp. grow and survive in spermicides. It has now been established by the applicant that certain lactobacilli which are, as discussed above, beneficial or protective bacteria, are spermicide resistant and can therefore be administered to female mammals who may be using or want to use a spermicide preparation, in order to treat or prevent urinary tract infections. By using the spermicide resistant strains of lactobacilli, the beneficial effect of treating urinary tract infections is not diminished or negated in situations requiring the intravaginal insertion of a spermicidal preparation.

Brief Summary Text (32):
A most preferred composition comprises one or more lactobacillus viable whole cells which are selected to be substantially spermicide resistant, a spermicide and a pharmaceutically acceptable carrier. This composition may be administered intravaginally or intraurethrally in the form of a cream, capsule, gel, paste or suppository. Alternatively, but equally effectively, the lactobacillus composition may be administered in a separate preparation from the spermicide, for example, after spermicide insertion.

Brief Summary Text (33):
Preferably, the lactobacillus is selected from the group comprising L. casei ss rhamnosus, L. casei ss alactosus, L . fermentum and L. brevis. Most preferably, the lactobacillus is either L. casei var rhamnosus GR-1 or L. fermentum B-54. Preferably, they are resistant to greater than 25% concentration of spermicide. The list provided herein is not intended to be exhaustive. A skilled technician with the present disclosure could readily determine other suitable substantially spermicide resistant lactobacilli.

Brief Summary Text (37):
2) requiring the use of a spermicide preparation benefit from this method and composition, but also female mammals not immediately in need of such treatment but who can be considered "prone" to urinary tract infections and who also require the use of a spermicide preparation. These individuals can benefit by treatment with both the spermicide resistant lactobacillus and the spermicide either separately or in one convenient preparation.

Brief Summary Text (38):
The ability of lactobacillus to exclude uropathogens from the urinary tract likely involves and is influenced by numerous factors and effects including:

Brief Summary Text (39):
1) the adherence of lactobacillus to uroepithelial or vaginal epithelial cells, and

Brief Summary Text (40):
2) the size of the lactobacillus. (Reid et al. 1987, Journal of Urology 138:330-335, the contents of which are incorporated herein by reference).

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Brief Summary Text (41):
Although the present invention is not bound by any one theory or mode of operation, it is believed that, at least to some degree, a combination of coaggregation of lactobacillus with uropathogens and the production by lactobacillus of one or more inhibitory substances may be responsible for excluding pathogens and/or reducing their numbers in the urinary tract.

Brief Summary Text (42):
From the standpoint of physical exclusion, the attachment of lactobacillus acts as a block to uropathogens by preventing access to receptor sites. Although complete exclusion of uropathogens theoretically can occur, the most common finding of the results of the present invention is that there is a reduction in uropathogen numbers compared to lactobacilli. In other words, although some lactobacilli may not completely exclude uropathogens, they are still capable of interfering with uropathogen colonization in vivo. Coaggregation is an important element as it allows lactobacilli to form a urogenital mixed flora present in healthy patients. This mixed flora is preferably dominated by lactobacilli and other indigenous gram positive bacteria. It is hypothesized that the lactobacilli of the present invention and some uropathogens coaggregate (Reid et al. 1988, Can. J. Microbiol. 34:344-351, the entire contents of which are incorporated herein by reference), in a way that interferes with the pathogenic process.

Brief Summary Text (43):
In one embodiment of the present invention, it may not necessary to use lactobacillus viable whole cells, non-viable whole cells or cell wall fragments. It has been found that lactobacillus exhibits an inhibitory activity on uropathogens which does not appear to be solely cell-associated. The factor or factors which are responsible shall be referred to as the inhibitory substance(s).

Brief Summary Text (44):
This inhibitory substance(s) may be readily separated from cultured lactobacillus cells by techniques such as filtration, precipitation and centrifugation which are readily known and applied in the art. The preferred techniques for the selection of the inhibitory substance(s) will be readily apparent to a skilled artisan from the detailed examples provided hereinbelow.

Detailed Description Text (7):
L. casei strains GR-1 and RG-17 and L. acidophilus were grown in brain heart infusion yeast extract media, human urine and human urine with 0.5% glucose and 0.5% lactose and were found to produce exopolysaccharide material and to attach well to uroepithelial cells in vitro (Cook et al. 1988, Current Microbiology 17:159-166). Endocervical, vaginal and periurethral epithelial cells from normal healthy pre-menopausal women also showed the presence of encapsulated lactobacillus attached to the cells. These results correlate the in vivo and in vitro data.

Detailed Description Text (9):
Different stages of the lactobacillus cell cycle were examined and adherence was found to occur best in the stationary phase of growth (Cook et al. Cur. Microbiol.). Capsule production was found in vitro and has also been noted in vivo (Reid et al. 1989).

Detailed Description Text (11):
There is a correlation between the receptivity of uroepithelial cells for bacteria/bacterial adherence to the cells in the in vivo and in vitro environment. Specifically, it has been found that lactobacillus adhesion to uroepithelial cells can a reflection of the in vivo adhesion of lactobacillus to the cells (Reid, 1988. Current Microbiology 18: 1989, pp. 93-97), although precise numbers may vary between patients.

Detailed Description Text (19):

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The following studies were designed to test specific lactobacillus isolates for their ability to competitively exclude common pathogenic bacteria from adhering to epithelial cells. An in vitro assay was designed which involved incubating lactobacilli with uroepithelial cells for 30 minutes at 37.degree. prior to incubation with the radiolabelled pathogens for 30 minutes at 37.degree.C., as described by Chan et al., Infection and Immunity, January 1985. The percentage inhibition caused by lactobacilli was measured from the numbers of radiolabelled organisms adhering to epithelial cells in test and control samples, as shown in Table 3.

Detailed Description Text (20):
The results demonstrate the ability of lactobacilli to competitively block pathogenic bacteria from adhering to epithelial cells, which demonstrates that lactobacillus strains can be used to prevent urinary tract infections. Studies have shown that L. casei GR-1 can detach uropathogens from uroepithelial cells (up to 45% detachment) supporting the use of lactobacilli in treating infections. This detachment is very important as it means that lactobacilli given to prone patients can remove uropathogens, adhere themselves, coaggregate and form a protective balance in the urogenital tract.

Detailed Description Text (22):
It is clear from Table 3 that although some lactobacilli did not completely exclude uropathogens, they are still responsible for the interference of uropathogen colonization in vivo. It has been found that this is due to many factors and may involve coaggregation between the lactobacillus and the uropathogens.

Detailed Description Text (24):
The results, which indicated that lactobacillus can coaggregate with E. coli and other uropathogens, has a bearing upon the importance of lactobacillus in vivo, particularly if inhibitor production accompanies coaggregation. These results also imply that the phenomena of coaggregation is of real clinical importance in the interaction of microorganisms in the urogenital tract.

Detailed Description Text (29):
The in vivo results seem to indicate that coaggregation of lactobacillus with potential uropathogens (gram-positive cocci and gram-negative rods) can result in a balanced ecological niche and a healthy status for the patient. Therefore, complete exclusion of uropathogens may not be necessary for protection from infection. This likely depends upon numerous factors, including host effects, as well as bacterial growth parameters and inhibitor production by specific lactobacillus strains.

Detailed Description Text (48):
The activity of the inhibitory substance produced by lactobacillus was studied in two phases in Reid et al. Can. J. Microbiol. 34:334-351 .

Detailed Description Text (50):
Various conditions were then tested for the expression of inhibitory activity including varying the concentration of the lactobacillus inoculum on the underlay, changing the conditions from aerobic to microaerophilic to anaerobic and varying the incubation temperature by heating the underlay to 80.degree. C. for 2 hours prior to innoculating with the indicator strain.

Detailed Description Text (52):
The second phase was undertaken to optimize the inhibitory effect and to determine whether it was solely due to a pH effect. For these studies, the effect of acid and pH were assessed by using nutrient agar as the underlay, resulting in a pH at 6.7 following lactobacillus growth. In addition, a 24-hour MRS culture filtrate of L. casei GR-1 neutralized with sodium hydroxide was assayed for activity against the uropathogens using a disc diffusion assay.

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Detailed Description Text (94):
The only child entered in this study was a 13- year-old girl who had a history of on average 20 documented lower UTIs per year since the age of 4. The infections were not related to sexual abuse, hygiene, bath irritants, or urinary tract abnormalities. Previous long- and short-term treatments with antibiotics had limited success and did not prevent recurrent coliform infections. Prior to lactobacilli instillation, her urogenital tract showed the presence of lactobacilli which did not inhibit her coliforms in vitro, but she was predominantly colonized with E. coli, as well as enterococci, coagulase-negative staphylococci, diphtheroids, and additional gram-positive cocci. She tolerated the lactobacilli instillations well and her mother noted a refreshingly healthy change in her appearance and attitude. The GR-1 colonized the vagina (110 bacteria/cell) and no coliforms were detected over a 6-week period. Due to an episode of gastroenteritis, not related to lactobacillus therapy, her treatment was discontinued.

Detailed Description Text (96):
The fifth patient was a 32-year-old mother of two with a 2-year history of irritative symptoms and persistent UTI, documented by cultures, and found to be mainly due to coliform bacteria. A strain of lactobacillus was isolated from her vagina, prior to therapy, and this had colony morphology distinct from L. casei GR-1 and showed no inhibitory activity in vitro against coliforms or enterococci. She tolerated the lactobacilli therapy and reported no adverse effects. The lactobacilli attached poorly to her vaginal epithelial cells (4 bacteria/cell) but existed as the dominant organism in the vagina for 4 weeks as found from the culture results. The vagina was consistently colonized also with enterococci, and these organisms caused a breakthrough symptomatic UTI which required antibiotics to eradicate. The patient re-entered the study with another 4-week infection-free period, but this was followed by another enterococcal infection. In an attempt to challenge the enterococci, a combination of L. casei GR-1 and L. acidophilus 76 (a high acid producing lactobacilli strain) was given. The lactobacilli colonization increased to 11 bacteria per vaginal epithelial cell and the patient became infection free for a further 4 weeks.

Detailed Description Text (98):
The lactobacilli colonized the vagina of the healthy control subject for up to 5 weeks after a single instillation. The patient's own lactobacillus strain also remained, but was not found to predominate.

Detailed Description Text (120):
Vaginal swabs were obtained from 44 premenopausal women with and without vaginitis, who used a variety of birth control methods. Smears from the swabs were Gram stained, examined for the presence of lactobacilli, and plated onto lactobacilli MRS agar (MRS) and brain-heart infusion agar supplemented with 2% yeast extract (BYE agar). The plates were incubated at 37.degree. C. for 18 h in 5% CO.sub.2. Organisms recovered from the plates were identified as lactobacilli with the API rapid CH kit and stored at -70.degree. C. in MRS broth plus 20% (wt/vol) glycerol. Freeze-dried lactobacillus isolates from the laboratory collection originally isolated from chicken, dairy and human sources were also cultured on MRS agar and broth.

Detailed Description Text (121):
Doubling dilutions of N-9 (Ortho Pharm., Canada) were made in MRS (pH 6.5) and BYE broth (pH 7.4) ranging from 0.1% to 25% (wt/vol). The pH of the N-9-supplemented medium was adjusted to the same level as unsupplemented medium where necessary. Lactobacillus isolates were subcultured three times prior to testing in the N-9 broths. The cultures were washed three times in phosphate-buffered saline, pH 7.1 (PBS), and resuspended to a concentration of 10.sup.7 cells mL.sup.-1. Aliquots of 50 uL were added to test tubes in triplicate containing 3 mL of either medium alone or medium plus N-9, mixed thoroughly, and incubated for 18 h at 37.degree. C. The tubes were scored for growth, and the M.I.C. was recorded as the lowest

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concentration demonstrating no growth. Aliquots of 50 uL were transferred from N-9/MRS tubes showing no growth to 3 mL of fresh MRS, incubated for 18 h at 37.degree. C., and examined for turbidity.

Detailed Description Text (123):
Accordingly, the fresh vaginal isolates of lactobacillus could be split into two groups according to their nonoxynol-9 minimum inhibitory concentrations: 67% (12/18) had minimum inhibitory concentrations for N-9 between 0.1% and 1.0%. The remainder grew in 25%, twice the maximum concentration used for contraceptive purposes. This latter group of lactobacilli were termed resistant.

Detailed Description Text (125):
The following microorganisms were deposited with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Md. 20852: Lactobacillus casei var rhamnosus GR-1, ATCC 55826 on Oct. 3, 1996; Lactobacillus rhamnosus GR-2, ATCC 55915 on Dec. 19, 1996; Lactobacillus rhamnosus GR-3, ATCC 55917 on Dec. 19, 1996; Lactobacillus rhamnosus GR-4, ATCC 55916 on Dec. 19, 1996; Lactobacillus jensenii RC-28, ATCC 55918 on Dec. 19, 1996; Lactobacillus rhamnosus RC-6, ATCC 55894 on Dec. 10, 1996; Lactobacillus rhamnosus RC-12,ATCC 55895 on Dec. 10, 1996; Lactobacillus rhamnosus A-60, ATCC 55896 on Dec. 10, 1996; Lactobacillus jensenii RC-11, ATCC 55920 on Dec. 26, 1996; L. casei var rhamnosus RC-17, ATCC 55825 on Oct. 3, 1996; and Lactobacillus fermentum B-54, ATCC 55884 on Nov. 26, 1996.

Detailed Description Paragraph Table (1):
TABLE 1 Lactobacilli per Growth media epithelial cell BYE Broth 62.68 BYE Tween 48.83 MRS Broth 48.40 BHI Broth 49.28 TS Broth 51.85 Urine 73.00 BYE Agar 63.78 BYE Tween 52.60 MRS Agar 48.13 BHI Agar 50.68 TS Agar 60.73 Rogosa's Agar 38.08

BYE = brain heart infusion medium (BBL Microbiology Systems, Becton Dickinson & Co. Cockeysville, U.S.A.). with 0.5% yeast extract; Tween = 0.1% Tween 80, (BBL, USA); MRS = Lactobacillus MRS medium (Difco USA); BH = brain heart infusion medium (BBL, USA); TS = trypticase soy (BBL, USA); Rogosa's = Rogosa SL, lactobacilli selective medium (Difco, USA).

Detailed Description Paragraph Table (3):
TABLE 3 Pathogenic Bacteria 1 2 3 4 5 6 Lactobacillus % Inhibition of attachment of pathogens L. casei GR-1 94 100 86 74 61 71 L. casei GR-2 84 81 100 58 59 79 L. casei GR-3 50 46 100 83 37 77 L. casei RC-9 57 28 NT NT 69 NT L. casei RC-21 NT 100 NT NT 14 NT L. Casei ATCC 7469 42 58 53 30 66 75 L. plantarum ATCC 8014 51 82 76 71 44 75 L. fermentum A-60 51 37 100 82 30 65 L. acidophilus T-13 42 0 21 74 0 63 L. fermentum B-54 39 0 53 50 0 64

1 = E. coli strain C121277; 2 = E. coli mannose sensitive strain; 3 = Proteus mirabilis strain 28cii; 4 = Klebsiella pneumoniae strain 3a; 5 = Pseudomonas aeruginosa mucoid; 6 = Pseudomonas aeruginosa nonmucoid; NT = not tested.

Detailed Description Paragraph Table (10):
TABLE 9 Minimum inhibitory concentration of N-9 for lactobacilli Minimum inhibitory Lactobacillus Number of concentration species strains <1.0% >25.0% Lactobacillus spp..sup.a 18 12 (67%) 6 (33%) L. acidophilus 12 8 (67%) 4 (33%) L. plantarum 2 1 (50%) 1 (50%) L. casei ss rhamnosus* 8 1 (13%) 7 *(88%) L. casei ss alactosus 1 0 (0%) 1 (100%) L. jensenii 3 3 (100%) 0 (0%) L. fermentum** 2 1 (50%) 1**(50%) L. brevis 1 0 (0%) 1 (100%) .sup.a Fresh vaginal isolates, not speciated. *includes GR1 **includes B54

Detailed Description Paragraph Table (11):
TABLE 10 Lactobacillus sensitivity to N-9: relationship to source of organisms Source of Number of lactobacilli isolates

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Sensitive.sup.a Resistant.sup.b _____ Vagina.sup.c 18 12 (67%) 6 (33%) Urogenital tract.sup.d 25 12 (48%) 13 (52%) Dairy 1 0 (0%) 1 (100%) Chicken 3 2 (67%) 1 (33%) Total 47 26 (55%) 21 (45%)
_____ .sup.a N-9 MIC <1% .sup.b N9 MIC >25% .sup.c Fresh clinical isolates .sup.d Stored laboratory strains

Other Reference Publication (7):
Reid et al. (1985) "Prevention of Urinary Tract Infection in Rats with an Indigenous Lactobacillus casei Strain", Infection and Immunity 49:320-324.

Other Reference Publication (8):
Wood et al. (1985) "In Vitro Adherence of Lactobacillus Species to Vaginal Epithelial Cells", Am. J. Obstet. Gynecol. 153:740-743.

Other Reference Publication (9):
Chan et al. (1985) "Competitive Exclusion of Uropathogens from Human Uroepithelial Cells by Lactobacillus Whole Cells and Cell Wall Fragments", Infection and Immunity 47:84-89.

Other Reference Publication (11):
Kleeman et al. (1982) "Adherence of Lactobacillus Species to Human Fetal Intestinal Cells", J. Dairy Sci. 65:2063-2069.

Other Reference Publication (12):
Klaenhammer (1982) "Microbiological Considerations in Selection and Preparation of Lactobacillus Strains for Use as Dietary Adjuncts", J. Dairy Sci. 65:1339-1349.

Other Reference Publication (15):
Will (1979) "Lactobacillus Overgrowth for Treatment of Moniliary Vulvovaginitis", The Lancet:482.

Other Reference Publication (16):
Friedlander et al. (1986) "Lactobacillus Acidophillus and Vitamin B Complex in the Treatment of Vaginal Infection", Pan Med. 28:51-53.

Other Reference Publication (17):
Scott (1961) "Treatment of Oral Disturbances by Lactobacillus Acidophilus", Bulletin of the Bronx County Dental Society XV, No. 4.

Other Reference Publication (18):
Alexander (1967) "Thrush Bowel Infection: Existence, Incidence, Prevention and Treatment, Particularly by a Lactobacillus Acidophilus Preparation", Curr. Med. Drugs 8:3-11.

Other Reference Publication (19):
Ehrlich (1963) "Treatment of Enteric Staphylococcic Infections with Lactobacillus Acidophilus", American Journal of Proctology.

Other Reference Publication (23):
Settel (1962) "Lactobacillus Acidophilus in the Treatment of Functional Gastrointestinal Disorders", Clinical Medicine 69:700-704.

Other Reference Publication (24):
Necheles (1961) "Beneficial Effects of Administration of Lactobacillus Acidophilus in Diarrheal and Other Intestinal Disorders", Am. J. Gastroenterology 35: 522-530.

Other Reference Publication (25):
Price et al. (1970) "Inhibition of Pseudomonas Species by Hydrogen Peroxide Producing Lactobacilli", J. Milk Food Technology 33:13-18.

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Other Reference Publication (26):
Read et al. (1966) "Lactobacillus Acidophilus (Enpac) in Treatment of Hepatic Encephalopathy", British Medical Journal 1:1267-1269.

CLAIMS:

1. A method for reducing the occurrence of urinary tract infections in a mammal which comprises administering a therapeutically effective amount of Lactobacillus viable whole cells.

2. The method of claim 1 wherein said lactobacillus is selected from group consisting of L. casei, L. acidophilus, L. plantarum, L. fermentum, L. brevis, L. jensenii and L. crispatus.

3. The method of claim 2 wherein said lactobacillus is L. casei.

4. The method of claim 2 wherein said lactobacillus is selected from the group consisting of L. casei var rhamnosus GR-1, L. casei var rhamnosus GR-2, L. casei var rhamnosus GR-3, L. casei var rhamnosus GR-4, L. casei var rhamnosus RC-17, L. casei NRC 430 and L. casei ATCC 7469.

5. The method of claim 2 wherein said lactobacillus is selected from the group consisting of L. acidophilus RC-12, L. acidophilus RC-25, L. plantarum RC-19, L. jensenii RC-11, L. acidophilus ATCC 4357, L. plantarum ATCC 8014 L. fermentum A-60 and L. fermentum B-54.

6. The method of claim 1 wherein said lactobacillus is spermicide resistant.

8. The method of claim 7 wherein said lactobacillus is selected from the group comprising L. casei ss rhamnosus, L. casei ss alactosus, L. fermentum and L. brevis.

9. The method of claim 8 wherein said lactobacillus is selected from L. casei var rhamnosus GR-1 and L. fermentum B-54.

10. A method for reducing the occurrence of urinary tract infections in a mammal which comprises coating at least part of a biologically compatible prosthetic device with a therapeutically effective amount of Lactobacillus viable whole cells, and contacting said device with the urogenital tract.

11. The method according to claim 10 wherein said lactobacillus is selected from the group consisting of L. casei, L. acidophilus, L. plantarum, L. fermentum, L. brevis, L. jensenii, and L. crispatus.

12. The method according to claim 11 wherein said lactobacillus is selected from the group consisting of L. casei var rhamnosus GR-1, L. casei var rhamnosus GR-2, L. casei var rhamnosus GR-3, L. casei var rhamnosus GR-4, L. casei var rhamnosus RC-17, L. casei NRC 430 and L. casei ATCC 7469.

13. The method according to claim 11 wherein said lactobacillus is selected from the group consisting of L. rhamnosus RC-12, L. jensenii RC-11, L. acidophilus ATCC 4357, L. Plantarum ATCC 8014 L. fermentum A-60 and L. fermentum B-54.

15. The method according to claim 10 which additionally includes coating at least a portion of the urogenital tract with an amount of one or more of the lactobacillus viable whole cells, non-viable whole cells and cell wall fragments prior to inserting said device into the urogenital tract.

16. A pharmaceutical composition suitable for reducing the occurrence of urinary tract infections in a mammal, which comprises an effective amount of at least one

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of a Lactobacillus selected from the group consisting of L. casei var rhamnosus GR-1, L. casei var rhamnosus GR-3, L. casei var rhamnosus 4, L. casei var rhamnosus RC-17, L. casei NRC 430, L. casei ATCC 7469, L. rhamnosus RC-12, L. acidophilus RC-25, L. jensenii RC-11, L. acidophilus ATCC 4357, L. plantarum 8014, L. fermentum A-60, and L. fermentum B-54 and a pharmaceutically acceptable carrier.

18. The method of claim 1 wherein said lactobacillus is selected from the group consisting of L. casei var rhamnosus GR-1, L. acidophilus 76 and L. fermentum B-54.

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